

# OPTIMUM GUIDANCE OF COMPLEX PCI BY CORONARY PRESSURE MEASUREMENT

Coronary disease

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In 1993, 1450 coronary interventions were performed in the Catharina Hospital in Eindhoven, the Netherlands. At that time, due to financial restraints, stents were not available. After two years of follow up, the reintervention rate in that population was 28%. In 1998, stents were available unrestrictedly in the same hospital and 1790 coronary interventions were performed. In that year, stents were implanted in 70% of the procedures and the reintervention rate after two years was 21%. In other words, comparing the pre-stent era with the stent era showed that the reintervention rate in the complete percutaneous coronary intervention (PCI) population in our hospital decreased from 28% to 21%. Thus, the reintervention rate in the stent era had decreased by 25% compared to the pre-stent era.

While this decrease in the reintervention rate is not small, it is not that large either. It means that the re-intervention rate today is in the range of 20% if a completely unselected “true life” patient population is considered. And it is beyond doubt that the interventional community has eagerly waited for further developments to decrease this 20% reintervention rate.

Recently, we have witnessed the dawn of what might be a new era—the era of drug eluting stents.<sup>1 2</sup> It will be unrealistic to suppose that the restenosis rate of these new stents will be zero. But if they fulfil only half of their promise, this would be a great step forward and be of major importance for interventional cardiology. Let us suppose that the restenosis rate of these drug eluting stents will be very low indeed, somewhere in the range of 10% at 1–2 years, and that no major unexpected long term side effects will occur. What will be the consequences for the practice of interventional cardiology?

Most likely, such a development will result in an extension of the PCI population to include more complex disease. Such a trend is already being observed. Patients with multiple abnormalities in one or more coronary arteries—classical candidates for bypass surgery today—will be more frequently selected for treatment by multivessel coronary intervention; even patients with diffuse disease, with or without superimposed focal lesions, may become candidates for PCI. In these groups of patients in particular, the question arises of how to use the new stents in the best possible way.

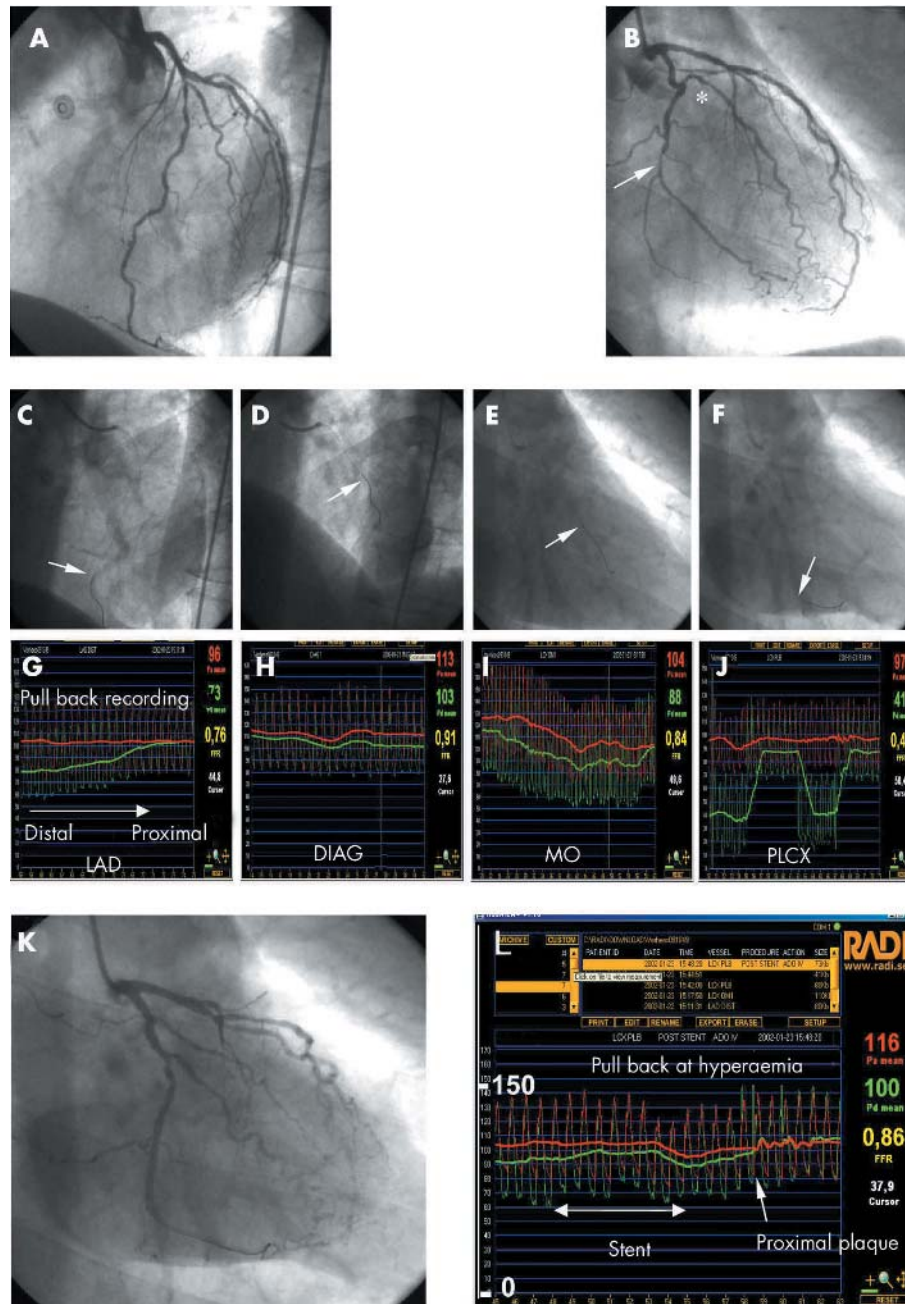
## MULTIVESSEL PCI: OUTLINING THE PROBLEM

The difficulties and dilemmas facing interventionalists considering multivessel PCI are illustrated in the four cases shown in figs 1–4.

Figure 1 shows the left coronary artery of a 57 year old man with class III angina and a positive exercise test, referred for PCI without a clear idea of where exactly PCI should be performed. Looking at the angiogram carefully, it is clear that this patient has angina and inducible ischaemia. There is diffuse disease along all the coronary arteries with a number of focal abnormalities superimposed on the diffuse disease. There are several narrowings in the left anterior descending (LAD) artery, in the obtuse marginal branch, and in the posterolateral branch of the circumflex artery. It is not difficult to point to at least six possible spots in this coronary tree where an intervention could be considered. However, it is impossible to conclude from the angiogram alone if this patient will be helped by a coronary intervention, and, if so, how to select the correct locations to intervene.

An identical problem is present in the patient in fig 2, a 60 year old man with extended multivessel disease who underwent a stent implantation in the right coronary artery one year earlier and who presented with recurrent typical angina and a positive nuclear perfusion imaging test in the inferior wall. The patient was initially classified as having three vessel disease and referred to our centre for bypass surgery. In the mid LAD artery there is a 50% stenosis (panel A), in a small left circumflex (LCX) branch there is a 90% stenosis, and in the right coronary artery (RCA) there is a 50% in-stent restenosis; however, there are also at least two other angiographically significant lesions and several less critical plaques, superimposed on diffuse disease (panel F).

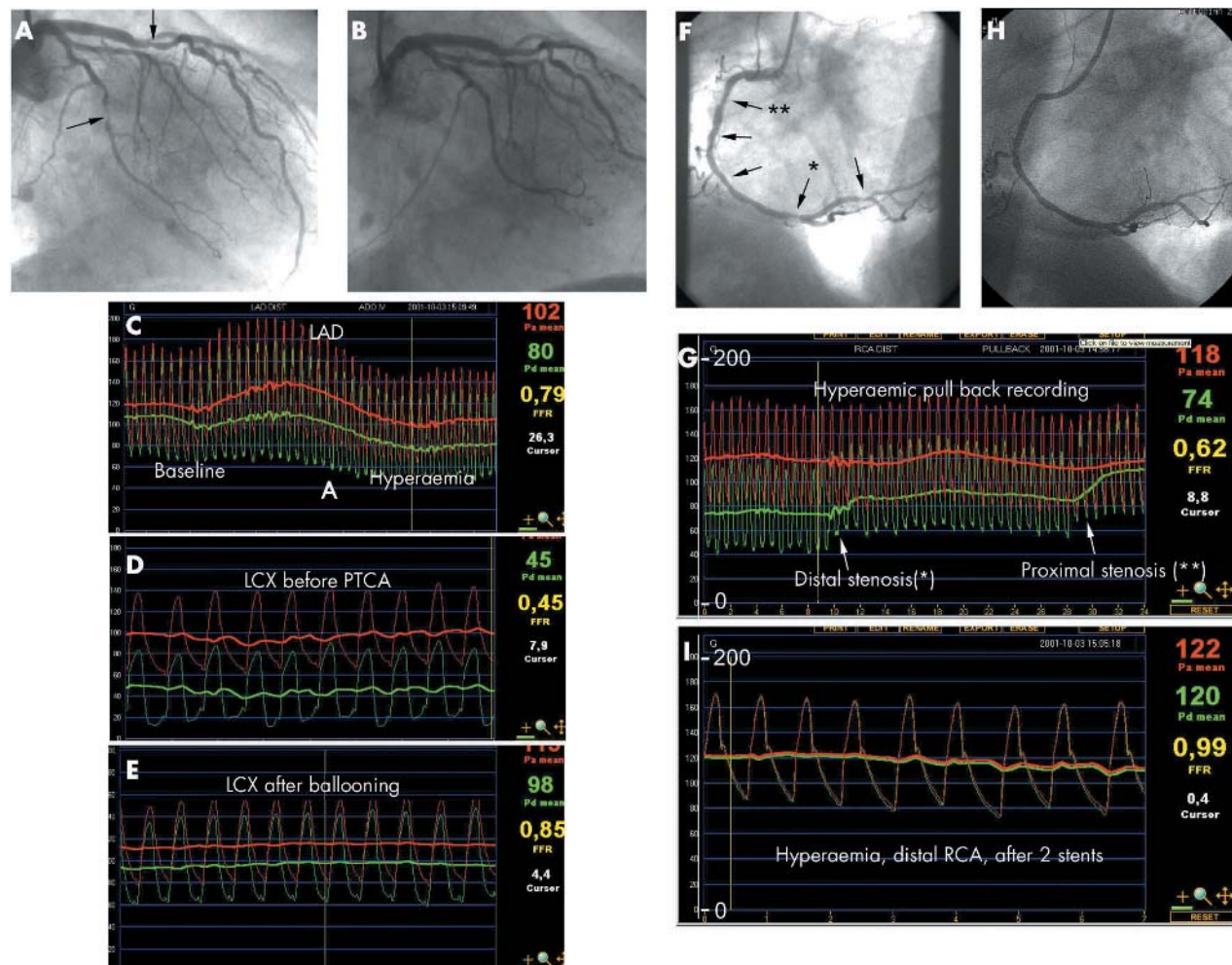
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**Figure 1** Angiograms and coronary pressure recordings in patient 1 described in the text. Panels A and B: left anterior oblique and right anterior oblique view of the left coronary artery. Multiple plaques and abnormalities are present along the arteries and superimposed on diffuse disease. Panels C to F and G to J: position of the pressure wire and pressure measurements during adenosine induced hyperaemia in the different branches of the left coronary artery. Fractional flow reserve (FFR) of the left anterior descending (LAD) artery, diagonal branch, obtuse marginal branch, and posterolateral branch are 0.76, 0.91, 0.84, and 0.42, respectively. Panel G shows that in the LAD there is not one or two single spots responsible for the decreased FFR, but that there is diffuse disease (gradual decline of pressure) along the complete coronary artery. Panel I shows the pull back curve from the obtuse marginal branch (identifying a discrete but non-significant stenosis in the proximal part of that branch). In panel J the sensor is moved across the stenosis in the posterolateral branch (PLCX) and back again several times, thereby precisely indicating the significant stenosis in that artery. Based upon the pressure measurements, the PLCX was stented. Panel K: Posterolateral branch after stenting. Panel L: pressure recordings in PLCX after stenting. Although FFR is still not normal, there is only a minor decline of pressure of a few mm Hg across the stent and the remaining gradient is caused by the more proximal plaque in the PLCX, shortly after the bifurcation with the obtuse marginal branch.

How do we proceed with the patient shown in fig 2 and select the optimum treatment? Considering the possibility of reintervention in the RCA, there are many locations along this coronary artery that could be considered to be stented, but evidently that is not a realistic option for all of them.

In fig 3, this patient presented with typical chest pain, a positive nuclear test in the inferior wall, and a severe long lesion in the RCA. There is no doubt that this lesion is responsible for ischaemia and the patient was referred for PCI of this stenosis. No interventionalist could be blamed for



**Figure 2** Left coronary artery of patient 2 described in the text. In the left coronary artery, there is a 50% stenosis in the mid left anterior descending (LAD) artery with a fractional flow reserve (FFR) of 0.79 (panels A and C). Furthermore, there is diffuse disease along the left coronary artery and a focal stenosis in the small circumflex branch (LCX), which is significant according to an FFR of 0.45 (panels A and D). After plain balloon angioplasty of the LCX stenosis, there is a satisfying angiographic result and the FFR has almost doubled to 0.85 (panels B and E). The right coronary artery shows diffuse disease with at least five stenoses of intermediate severity (panel F). FFR of the distal myocardium supplied by the right coronary artery (RCA) is 0.62 (panel G). The pressure pull back curve at hyperaemia shows that two of these multiple plaques are haemodynamically significant (asterisks). The other plaques do not have haemodynamic significance. Consequently, two stents were placed at the locations indicated by the asterisks whereafter a reasonable angiogram and an excellent functional result was obtained with normalisation of FFR (panels H and I).

stenting this RCA stenosis. But is that the complete story? Also, the bifurcation of the left main is not completely normal, with plaques in both the LAD and LCX arteries. What is the best treatment for this patient? Just stenting the right coronary artery or examining the left artery further?

Finally, fig 4 shows the coronary angiogram of a 57 year old man, referred for brachytherapy of an in-stent restenosis in the right coronary artery (panels A and B). The patient had received a stent three years earlier, was free of symptoms thereafter, but had recurrent angina for the last two months with a positive nuclear scan in the inferior wall. But is there an in-stent restenosis, and therefore is brachytherapy indicated? There are also three plaques in the LAD, although angiographically not significant (panel D). The presence of reversible ischaemia in the apex on the MIBI scan could also be explained by the LAD, reaching far across the apex.

How should we proceed? Just “blindly” irradiate the RCA with the risk of activating a quiet, non-significant lesion? Or try to get some more specific information beforehand about

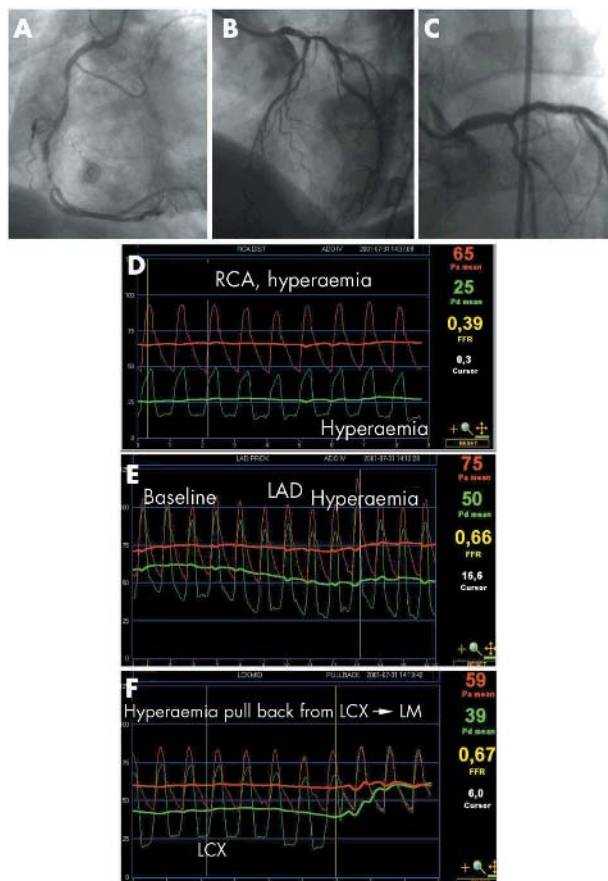
the individual lesions? How can such essential information be obtained?

## HOW TO SELECT THE CULPRIT LESIONS

All four patients presented here share a number of common features: all of them have both focal lesions and long segments with diffuse disease. They have multiple spots or segments that could be held responsible for their complaints and for the ischaemia. In all of them, the key issue is whether they can be treated by PCI at all and, if so, how to perform an optimal selection of those spots or segments to be treated. How many stents should be implanted and where should those stents be placed? Should long or short stents be used? Or should such patients be treated by coronary artery bypass surgery, or even medically?

As previously stated, with the introduction of drug eluting stents with anticipated lower restenosis rates, those patients described above will become more common in the population referred for intervention. We need to answer all of these





**Figure 3** Angiograms and pressure recordings in a patient with typical chest pain, a positive nuclear test in the inferior wall, and a severe stenosis in the right coronary artery with a fractional flow reserve (FFR) of 0.39 (panels A and D). However, on the angiogram of the left coronary artery, suspicion is raised with respect to the left main artery (panels B and C). Pressure recordings in the left anterior ascending artery and left circumflex artery (LCX) clearly show that the left main stenosis is significant, with an FFR of 0.66 (panels E and F). The lower panel F also shows the pull back of the pressure sensor from the LCX to the left main artery, precisely indicating the site of haemodynamic obstruction at the end of the left main artery.

questions to ensure maximal benefit for our patients, at an affordable cost.

One thing can be stated with certainty: it is neither wise nor feasible to implant an unlimited number of stents in these patients, for several reasons. First, the advantage of reducing the re-intervention rate will disappear. If the restenosis rate is only 10% for one drug eluting stent, this means a restenosis rate of 28% for three stents and 36% for four stents. Secondly, making a metal cast of a coronary artery is undesirable and will disturb flow, affect perforating branches, and have a negative influence on normal physiology. Thirdly, the treatment will become extremely expensive and future treatment by bypass surgery will be very difficult. Last but not least, it has been repeatedly demonstrated in these patients that only haemodynamically significant stenoses need to be treated and that dilatation of functionally non-significant lesions is of no benefit and should be avoided.<sup>3-6</sup>

It is the presence and extent of inducible ischaemia which determines the prognosis in these patients, not the angiographic extent of disease. PCI at the correct locations is

directed at abolishing symptoms caused by myocardial ischaemia; improving prognosis and longevity requires other approaches such as lipid lowering treatment.

Therefore, for an optimum benefit from drug eluting stents in patients with complex disease and multiple abnormalities, it is mandatory to make a strategic selection of those arteries and/or locations/segments/spots where stenting will be most effective. This means that detailed spatial, focal, and segmental information about the functional impact of all the abnormalities is required. Which of several possible lesions are “culprit”? Can we select particular spots or segments within a coronary artery which are of haemodynamic importance? Is it focal epicardial disease or diffuse disease or even microvascular disease that causes the ischaemia? It is clear that the methodology to answer these questions is of major importance.

Unfortunately, such detailed segmental information cannot be obtained by any classical non-invasive or invasive methodology (table 1). High quality nuclear perfusion imaging can identify the culprit artery but does not give segmental information in the case of several abnormalities within the same artery,<sup>7,8</sup> nor does it distinguish diffuse epicardial disease from focal stenosis. Quantitative coronary angiography (QCA) is not even reliable in assessing the functional significance of a single stenosis, let alone multiple or complex abnormalities.<sup>9,10</sup> Intravascular ultrasound (IVUS) in such patients will show disease everywhere along the coronary artery without providing functional information on the distinct lesions. With Doppler flow imaging, no discrimination can be made between the abnormalities within the artery or between the epicardial and microvascular disease.<sup>11,12</sup>

In contrast, coronary pressure measurement gives the answer to those questions, as will be clarified below.

## FRACTIONAL FLOW RESERVE

Fractional flow reserve (FFR) is defined as the ratio of maximum blood flow in a diseased artery to maximum flow if the same artery would be normal. Stated another way, maximum flow in the presence of the stenosis is expressed as a fraction of maximum flow in the hypothetical case that the epicardial artery is completely normal.<sup>13-15</sup>

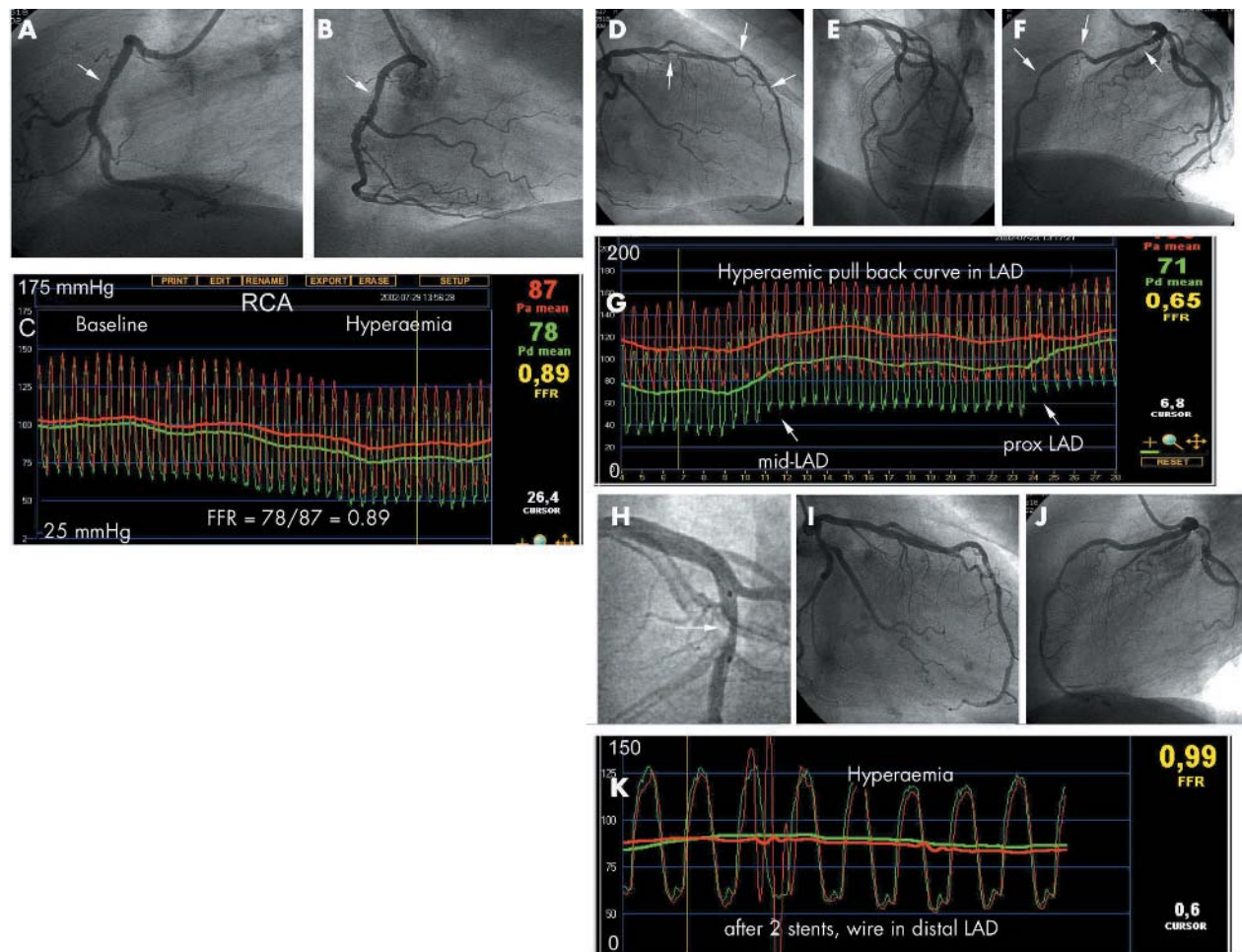
The concept of FFR is explained in fig 5.

In contrast to most other invasive indexes, FFR has a direct clinical equivalence: FFR of 0.60 means that the maximum amount of blood (and oxygen) supplying that particular myocardial distribution only reaches 60% of what it would be reaching if the respective artery were completely normal. An increase to 0.90 after coronary intervention indicates that maximum blood supply has now increased by 50%.

The characteristics of FFR have been extensively described and validated over recent years (table 2). FFR can be calculated by taking the ratio of mean distal coronary pressure to aortic pressure during maximum coronary hyperaemia,<sup>13-15</sup> when myocardial resistance is minimal and constant, and when maximum blood flow is directly proportional to myocardial perfusion pressure (Pd-Pv).

Maximum hyperaemia can be achieved by intracoronary adenosine or papaverine administration or by intravenous infusion of adenosine (table 3).

FFR has an uniform normal value of 1.0 for every patient and every coronary artery; it is not dependent on changes in heart rate, blood pressure, or contractility; it accounts for collateral flow; and it has a sharp threshold value to indicate



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**Figure 4** Angiogram and pressure tracings of a 57 year old man referred for brachytherapy of a supposed in-stent restenosis in the right coronary artery (panels A and B). The stent was placed in the mid right coronary artery (RCA) three years earlier. According to the pressure measurements, however, the stenosis is not significant at all and a fractional flow reserve (FFR) of 0.89 three years after stenting indicates an excellent functional result at present (panel C). The patient had ischaemia on the nuclear scan in the inferior wall. Could the ischaemia also be explained by the left coronary artery, reaching across the apex? In the left anterior descending (LAD) artery there are three plaques (panels D, E, and F) and when the pressure wire is placed in the distal LAD and hyperaemia is induced, FFR of this artery is significantly decreased to 0.65 (panel G). Making the hyperaemic pull back recording, it can be clearly seen that there are two focal spots within the LAD which are the culprit lesions from a haemodynamic point of view. Panel H shows the proximal plaque more clearly just before stent inflation, and panels I and J show the final angiographic result after stenting both culprit spots. In panel K the final pressure recordings are made, showing that FFR has normalised after stenting these two plaques.

inducible ischaemia;  $\text{FFR} < 0.75$  always indicates inducible ischaemia;  $\text{FFR} > 0.80$  excludes ischaemia in 90% of the cases. The grey zone is very limited, which is important for clinical decision making in an individual patient.

Coronary pressure measurements can be easily performed by pressure wires, with almost identical mechanical properties as normal guide wires, and barely prolong the procedure, even when multiple vessels are interrogated.<sup>16–19</sup>

A successful measurement of FFR can be performed in 99% of the arteries and the measurements are highly reproducible.<sup>15</sup> More recently the prognostic value of FFR post-stenting was demonstrated in a large multicentre study in 750 patients. Normalisation of FFR after stent placement (thereby restoring normal conductance of the artery) was accompanied by a restenosis rate of less than 5% at six months follow up, with a strong inverse relation between post-stent FFR and event rate.<sup>19</sup>

Recently, multivessel PCI guided by pressure measurement was compared to bypass surgery and yielded a

similarly favourable outcome, not only in terms of adverse events but also in terms of reinterventions and quality of life.<sup>5</sup>

The usefulness of coronary pressure measurement has been demonstrated in a variety of pathological situations including unstable angina and in the subacute phase after a previous infarction.<sup>17–20</sup> In the case of an acute myocardial infarction, coronary pressure measurement is less reliable, at least for the infarcted area.

Finally, the unique and most powerful application of coronary pressure measurement is the performance of the pressure pull back curve which unambiguously discriminates any functional abnormality along the course of a coronary artery, as will be clarified below.<sup>17–18</sup>

## WHERE TO PLACE OUR STENTS

The answers to the diagnostic questions posed by the four patients described above are provided by the so called coronary pressure pull back recording.<sup>5 14 15 17–19</sup>

**Table 1** Limitations of different methods to select the culprit lesion(s) in multivessel disease**Nuclear scintigraphy**

- ▶ No discrimination between several abnormalities within one coronary artery
- ▶ More severely diseased area masks other ischaemic areas
- ▶ False negative in cases of balanced disease
- ▶ Needs to be performed in another department

**Quantitative coronary angiography**

- ▶ Rapid, cheap, reproducible, no additional equipment needed, but...
- ▶ Poor correlation with flow impairment in individual lesions
- ▶ Reference segment often not normal in multivessel disease

**Doppler flow imaging**

- ▶ Large overlap between normal and pathologic values
- ▶ Strongly influenced by changes in heart rate and blood pressure
- ▶ No discrimination between several abnormalities, between diffuse and focal epicardial disease, or epicardial and microvascular disease
- ▶ Often frustrating and time consuming

**Intravascular ultrasound**

- ▶ Unequalled structural information about plaque and wall, but...
- ▶ In extended multivessel disease, IVUS shows disease everywhere and fails to give the necessary functional information about which individual lesions may be "culprit"
- ▶ Expensive, long learning curve, additional equipment mandatory, relatively time consuming

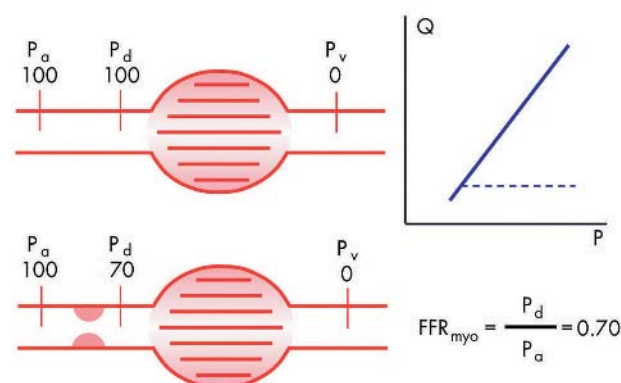
**Table 2** Features of fractional flow reserve (FFR)

- ▶ Normal value = 1.0 for every patient and every artery
- ▶ FFR is not influenced by changing haemodynamic conditions (heart rate, blood pressure, contractility)
- ▶ FFR specifically relates the influence of the epicardial stenosis to the myocardial perfusion area and blood flow
- ▶ FFR accounts for collaterals
- ▶ FFR has a circumscribed threshold value (~0.75–0.80) to indicate ischaemia
- ▶ FFR is easy to measure (success rate 99%) and extremely reproducible
- ▶ Pressure measurement has an unequalled spatial resolution (pressure pull back recording)

Let us have a closer look at these four patients and see how the necessary and relevant information could be obtained by coronary pressure measurement.

**Patient 1**

In the patient in fig 1, the pressure wire was placed in the distal part of the left anterior descending artery, the diagonal



**Figure 5** Concept of fractional flow reserve (FFR): during maximum arteriolar vasodilation, the resistance of the myocardium is minimal, therefore maximum myocardial blood flow is proportional to hyperaemic perfusion pressure which equals  $P_d - P_v$ . Because there is no decline of pressure along a normal coronary artery,<sup>13</sup> and neglecting  $P_v$ , this means that if the epicardial artery was completely normal, perfusion pressure at hyperaemia equals  $P_a$ . In the presence of a stenosis, hyperaemic perfusion pressure has decreased to  $P_d$ , therefore maximum flow in the presence of the stenosis as a ratio (fraction) of normal maximum flow is represented by the ratio of perfusion pressures:  $P_d/P_a$ . This fraction of normal maximum flow, which is maintained despite the stenosis, is called FFR. For further explanation see text, and Pijls and colleagues.<sup>13 14</sup>

branch, the obtuse marginal branch, and the posterolateral branch, respectively (panels C to F), and corresponding pressure tracings were made at baseline and hyperaemia (panels G to J). As can be seen, FFR in the LAD artery is 0.76 which is a borderline value and could mean that some ischaemia could be caused by that artery (panel G).<sup>13 14 17</sup> When making the pull back curve, however, the pressure decline along that artery was very gradual without a sudden pressure drop. This means that it is not possible to do any meaningful percutaneous intervention in this artery. Medical treatment is the best remedy for the vessel. The FFR in the diagonal artery was 0.91 (panel H). That is well above the ischaemic threshold of 0.75–0.80 and therefore this vessel cannot be held responsible for the ischaemia at exercise testing. The pressure recording in the stenotic marginal branch (panel I) shows an FFR of 0.84, also clearly above the ischaemic threshold, and making reversible ischaemia caused by this vessel also unlikely. In contrast to the LAD, where a diffuse decline in pressure is present, in the obtuse marginal (MO) branch a very localised pressure drop is observed when the sensor is pulled back across the proximal MO branch.

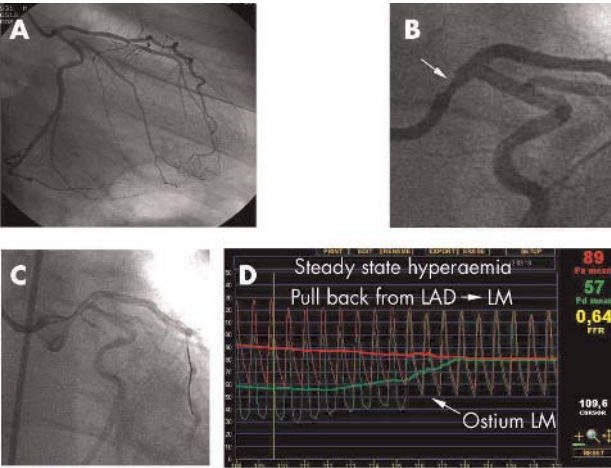
Finally, FFR in the posterolateral branch was severely depressed, although only a 50% stenosis was present in that vessel (panel J). It can be seen how a very local pressure drop occurs and disappears when pushing up and pulling back the pressure sensor. It is clear that this is the culprit lesion and an intervention at the particular location where that pressure drop occurs is indicated. After having stented this vessel (panel K), an FFR value of 0.86 is obtained which in itself is not very high after stenting.<sup>19</sup> But by making a pull back curve (panel L), it can be observed that there is very little gradient across the stent and that the remaining gradient originates at the other plaque in the ostium of this

**Table 3** Maximum vasodilating stimuli

- ▶ Papaverine ic (10 mg RCA, 15–20 mg LCA)
  - ▶ Adenosine or ATP ic (30  $\mu$ g RCA, 40–80  $\mu$ g LCA)
  - ▶ Adenosine or ATP iv (140  $\mu$ g/kg/min in large vein)
- Note**
- ▶ Maximum hyperaemia is paramount to determine FFR
  - ▶ Sometimes, incremental doses of ic adenosine or ATP might be necessary
  - ▶ Intravenous adenosine or ATP preferably by femoral vein (most reliable and quickly) or large antecubital vein

ATP, adenosine triphosphate; FFR, fractional flow reserve; ic, intracoronary; iv, intravenous; LCA, left coronary artery; RCA, right coronary artery.





**Figure 6** Technique of pressure pull back recording in a suspicious ostium. A 71 year old patient referred for percutaneous coronary intervention (PCI) of a diagonal coronary artery in which the pressure wire was used as a routine wire (panel A). When crossing the left main, a pressure gradient was observed giving rise to the suspicion of ostial stenosis. Additional angiograms were made as shown in panel B. The pressure pullback recording was made to analyse the ostial lesion (panels C and D), confirming the presence and exact location of a large gradient at the ostium of the left main coronary artery. Note that the guiding catheter is slightly withdrawn from the ostium during the pull back recording and that hyperaemia was induced by intravenous adenosine. Obviously, the patient was switched from PCI to bypass surgery.

posterolateral branch. So, the result was accepted and up to now (two years later) the clinical course was uneventful.

**Patient 2**

In the second patient (fig 2), FFR was measured initially in the LAD artery with a value of 0.79, indicating that this vessel most likely is not significantly diseased and that the patient has two vessel and not three vessel disease (panels A and C). FFR in the posterolateral branch (not surprisingly) is severely depressed at 0.45 (panel D). After balloon treatment, it increased to a value of 0.85, which was accepted in this case because the vessel is small and using a traditional stent would have a rather high risk for in-stent restenosis (panel E).

However, matters become really interesting when looking at the RCA and making the pull back curve during maximum hyperaemia in that artery. With the sensor in the distal RCA, an FFR of 0.62 is measured, a clearly ischaemic value (panel G). This means that all the abnormalities along the right coronary artery were grouped together, resulting in a significant decrease of maximum blood flow along this artery. When the pull back is made in this artery, it can be clearly seen that there are two particularly discrete locations responsible for the pressure drop, one of them the stenosis before the crux and one of them being the proximal plaque. Therefore, in this patient it can be concluded that blood flow can be largely restored by just treating these two spots and leaving the other plaques untreated. Also the previously stented lesion in the mid RCA obviously does not have any haemodynamic influence and brachytherapy of that stented area is not necessary. Two stents were placed in this RCA at the respective locations of pressure drop, whereafter FFR normalised (panels H and I).

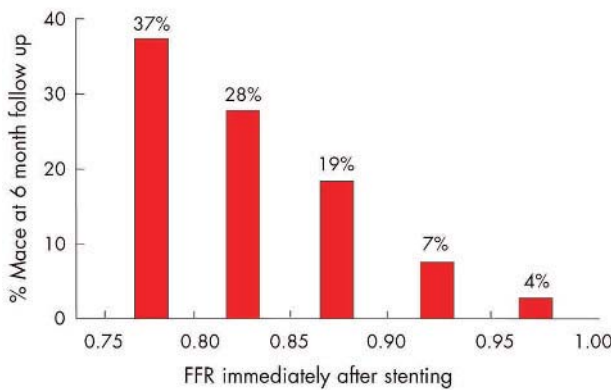
**Table 4** The pressure pull back recording

- ▶ Place sensor in distal coronary artery
  - ▶ Induce sustained maximum hyperaemia by intravenous adenosine, or intracoronary papaverine
  - ▶ Pull back the sensor slowly under fluoroscopy
  - ▶ If a focal pressure drop is present, it can be confirmed by moving the sensor across the stenosis and back again
  - ▶ The individual contribution of every segment and spot to the extent of disease can be studied in this way and the correct position to place the stent(s) can be unequivocally determined
  - ▶ In case of multiple spots considered to be stented, the pull back curve can be repeated after every step
  - ▶ In case of a gradual decline of pressure along the artery, without focal pressure drops, stenting makes no sense and medical treatment is indicated
- Coronary pressure is unique in this respect and such detailed spatial information cannot be obtained by any other invasive or non-invasive method**

**Patient 3**

The pressure measurement in the RCA of patient 3 (fig 3) showed a very low FFR of 0.39 as expected (panel D). However, the left main (LM) bifurcation stenosis is also haemodynamically significant as clearly shown by placing the pressure sensor in the LAD and the LCX branches and measuring FFR (0.66 and 0.67, respectively; panels E and F). The pullback recording from the LCX to the LM unambiguously shows the severe functional stenosis at the end of the LM artery. Obviously, the MIBI scan was false negative in the anterolateral wall simply because the perfusion abnormality was more severe in the RCA territory, thereby masking the less severe but significant hypoperfusion in the LCA territory.

Masking one ischaemic area by the more severe perfusion defect in another area is one of the limitations of perfusion scintigraphy in multivessel disease.<sup>8</sup> If treated according to the non-invasive and angiographic standards by placing a stent in the RCA, this patient would have returned to the outpatients clinic still complaining of exercise induced chest pain. In the best case, MIBI would have been repeated and



**Figure 7** Relation between fractional flow reserve (FFR) after stenting and major adverse cardiac event (MACE) rate at follow up.<sup>19</sup> Distribution of the study population over five FFR categories. A strong inverse correlation was present between FFR after stenting and event rate at six months follow up, despite similar angiographic results in all five categories.



**Figure 8** Set up in the catheterisation laboratory of the Catharina Hospital, Eindhoven. On the right side, from top to bottom, a bag filled with adenosine for intravenous infusion, the adenosine infusion pump, and the Radi Analyzer are mounted and fixed to the table for immediate use if requested.

would have indicated a reversible perfusion defect now in the anterior and lateral wall, and bypass surgery would have been performed. In the worst case, the angiogram would have been repeated directly, possible intimal hyperplasia in the stent would have been misinterpreted as restenosis and irradiated, leading to further high costs without appropriate treatment.

#### Patient 4

Finally, in patient 4 (fig 4), pressure measurement showed an FFR of 0.89 in the RCA, excluding significant in-stent restenosis (panel C). When investigating the LAD, however, both the insignificant plaque in the proximal LAD and the 50% stenosis in the mid LAD showed considerable pressure gradients together, resulting in an FFR value of 0.65 (panel G). After stenting those two spots, guided by the pressure pull back recording, FFR normalised completely to 0.99 (panels H to K). The decision to leave the RCA untreated, and to place two stents in the LAD, would probably never have been taken without the support of the pressure measurements.

#### TECHNIQUE OF THE PRESSURE PULL BACK RECORDING

Originally, the pressure wire was mostly used to analyse a single stenosis of intermediate severity.<sup>4 14</sup> In such cases, the sensor was placed distal to the stenosis and a single hyperaemic stimulus (most often intracoronary adenosine) could be given and FFR determined.<sup>24</sup> But as has been shown in the patients above, the potential information provided by the pressure measurements goes far beyond that and, especially in more complex disease, its optimum use includes making a pressure pull back recording (table 4).<sup>15–20</sup> To make such a recording, the sensor should be placed in the distal coronary artery and sustained maximum hyperaemia should be induced, either by intravenous adenosine or intracoronary papaverine (table 3).<sup>21</sup> This enables FFR measurement of the complete artery and informs the operator if inducible ischaemia related to that artery is present and warrants treatment. Thereafter, the sensor is simply pulled back by hand slowly under fluoroscopic guidance and the pressure

curves are recorded by the interface or by the regular catheterisation laboratory recording system (fig 1, panels I and J; fig 2, panel G; fig 3, panel F; fig 4, panel G). If desired, the wire can be pushed up and pulled back a little bit as soon as a pressure drop is observed to confirm the exact location of the drop (fig 1, panel J). In that way, the individual contribution of every segment and every spot to the extent of disease can be studied. As remarked above, coronary pressure is unique in this respect and such detailed spatial information cannot be obtained by any other invasive or non-invasive method. The pressure pull back curve is also particularly useful to evaluate difficult ostial lesions, often hard to recognise and interpret on the classical coronary angiogram as is the case in fig 6. In such a case, the pressure sensor can be placed in the coronary artery across the ostium, hyperaemia can be induced, and the guiding catheter can be slightly pulled out of the ostium. Thereafter, the sensor can be slowly pulled back as demonstrated in fig 6.

It has been shown that, even with classical stents, dedicated use of the pressure wire enables PCI in multivessel disease to be as effective as bypass surgery in many patients.<sup>5</sup> Therefore, it can be anticipated that with the combination of drug eluting stents and such dedicated pressure guided strategy, PCI will become more common in the majority of those patients.

An important issue is that the mechanical properties of the present generation pressure wire have been improved dramatically and in fact are no longer distinguishable from a regular high torque floppy guidewire. In a recent multicentre registry, successful measurement of coronary pressure could be achieved in 744/750 patients (99.3%) without complications.<sup>19</sup> Also the reproducibility of the method is very high.<sup>4 22</sup> In the multicentre DEFER study, the difference between paired measurements was  $3 \pm 2\%$ .<sup>4</sup>

Therefore, rapid and safe evaluation of multiple coronary arteries can be easily performed by those wires without much prolongation of the procedure and with more accurate decision making.

#### PROGNOSTIC IMPLICATIONS AND COST EFFECTIVENESS

Coronary pressure measurement is not only effective in selecting the correct spots and segments to stent, but also yields important prognostic information. It has been shown recently that, after stenting, a strong inverse correlation is present between FFR measured directly after stent implantation and the adverse event rate during follow up (fig 7).<sup>19</sup> This was not only the case for repeated coronary interventions but also for death and myocardial infarction rate. In patients in whom FFR completely normalised after stenting, the adverse event rate at six months was approximately 5%, compared to almost 20% in patients with FFR below 0.90.

Finally, because the pressure wire can be used as a first line guide wire, both the diagnostic information, the interventional procedure, and evaluation of the result can be obtained without the necessity of extra equipment and with minimal loss of time.

In this context, however, one should realise that “easy to use” means “ready to use”. Therefore, for optimum use of coronary pressure measurement, the equipment should be an integral part of the set up in the catheterisation laboratory, enabling measurements quickly if clinically indicated. The set up in the catheterisation laboratory of the Catharina Hospital in Eindhoven is shown in fig 8.



The cost effectiveness of using coronary pressure in complex PCI has been demonstrated recently in several studies.<sup>20–23</sup> In day-to-day practice, the savings will be much more exaggerated because the effect of placement of stents at correct locations instead of placement on a “trial and error” basis at different consecutive procedures is hard to include in such studies, but will result in dramatic savings. A more refined and individualised understanding of disease, and a more appropriate selection of the epicardial lesions to be treated in patients with complex disease, will be paramount not only for patient care but also to keep health care affordable.

## CORONARY PRESSURE, COMPLEX PCI, AND DRUG ELUTING STENTS: FUTURE PERSPECTIVE

In summary, if drug eluting stents fulfil half of their expectations, this will be an enormous step forward for interventional cardiology.

As a consequence, the population selected for PCI will extend to patients with more complex disease. However, to use such a blessing in the most beneficial way for our patients, sound clinical, physiological, and scientific analysis by the interventionalist is mandatory.

Because oversimplified multi-stenting will annihilate the benefits of these new stents and be unnecessarily expensive, the traditional “plumber mentality” of some interventionalists should be abandoned. A change in attitude of many operators will be necessary and it should be realised that old proverbs as “stent ‘em all” and “seal every plaque” do not reflect evidence based medicine and should be avoided.

Finally, coronary pressure measurement (and especially the pressure pull back recording) seems to be the ideal tool to guide complex interventions in patients with advanced atherosclerosis and, while not indicated in all cases, should become standard in at least the majority. It not only selects branches, spots, and segments where stent placement is most effective, but it also enables immediate evaluation of the result with prognostic implications at affordable costs.

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